

OXIDATIVE STRESS AND ANTI OXIDANTS STATUS IN PELLAGRA

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ABSTRACT

Background and objectives: Pellagra was vanished from most parts of the world where it was formerly present due to its dietary modification. However, it is still encountered among the jowar eating populations of India. The information about the role of oxidative stress in pellagra was not established. Therefore, in this study we assessed the oxidative stress status by using malondialdehyde (MDA), total anti oxidant status (TAOS) and redox ratio (RER) in clinically diagnosed pellagra patients. **Materials and methods:** Clinically diagnosed pellagra patients aged between 18 to 40 years, both male and females were recruited (n=78) from department of Dermatology. Age and gender matched controls (n=78) were recruited from the student and residents of the hospital. Malondialdehyde (MDA) is a marker of lipid peroxidation, Total Anti Oxidant Status (TAOS) and Redox Ratio (RER) markers were assessed by using commercially available kits. **Results:** There were no significant differences in the anthropometric parameters. However, the oxidative stress markers MDA (p<0.05), RER (p<0.001) were significantly high and TAOS was low (P<0.001) in pellagra patients in comparison with age and gender matched controls. **Conclusion:** The results of this study showed the increased MDA, RER levels and decreased TAOS levels. Estimation of these markers at early stage will help to take measures to prevent the progression of disease and develop antioxidant strategies.

INTRODUCTION

Pellagra is derived from the Italian "Pelle" means "skin" and "Agra" signifying "rough", in reference to its thickened rough skin. Pellagra has long been known to be a nutritional disorder caused by cellular deficiency of niacin, resulting from inadequate dietary supply of niacin and tryptophan^[1].

Pellagra has been reported from most parts of the world where maize is consumed as a staple diet. Since the Second World War, pellagra was vanished from most parts of the world where it was formerly present due to its dietary modification. However, it is still encountered among the jowar eating populations of India^[2].

Oxidative stress is defined as a "state in which oxidation exceeds the antioxidant systems in the body secondary to a loss of the balance between them"^[3]. It not only causes hazardous events such as lipid peroxidation and oxidative DNA damage, but also physiologic adaptation phenomena and regulation of intracellular signal transduction. Oxidative stress plays a pathological role in the development of various diseases including diabetes, atherosclerosis, or cancer. Systemic oxidative stress results from an imbalance between oxidants derivatives production and antioxidants defenses. Reactive oxygen species (ROS) are generally considered to be detrimental for health. However, evidences have been provided that they can act as second messengers in adaptative

responses to stress. Obesity represents a major risk factor for deleterious associated pathologies such as type 2 diabetes, liver, and coronary heart diseases. Many evidences regarding obesity-induced oxidative stress accumulated over the past few years based on established correlations of biomarkers or end-products of free-radical-mediated oxidative stress with body mass index. The hypothesis that oxidative stress plays a significant role in the development of metabolic disorders, especially insulin-resistance state, is supported by several studies where treatments reducing ROS production reverse metabolic alterations, notably through improvement of insulin sensitivity, hyperlipidemia, or hepatic steatosis^[4].

However, the information about the role of oxidative stress in pellagra was not established. Therefore, in this study we assessed the oxidative stress status by using malondialdehyde (MDA), total anti oxidant status (TAOS) and redox ratio (RER) in clinically diagnosed pellagra patients.

MATERIALS AND METHODS

Study design: Analytical study

Ethics approval: This study was approved by Institute Ethics Committee, written inform consent was obtained from all the participants.

Inclusion criteria: Clinically diagnosed pellagra patients aged between 18 to 40 years, both male and females were recruited (n=78) from department of Dermatology. Age and gender matched controls (n=78) were recruited from the student and residents of the hospital.

Exclusion criteria: Patients suffering from chronic hypertension, diabetes mellitus, coronary artery diseases and other diseases were excluded. Age and gender matched controls were recruited among residents and staff of our hospital.

Sample size: one hundred fifty six.

Grouping: Group 1: Pellagra patients (n=78), Group 2: Control (n=78).

Methodology: Age, gender, height, weight were recorded for all the participants. The medical chart was reviewed for clinical characteristics, such as hypertension, diabetes, coronary artery disease etc., 5ml of blood was collected under aseptic conditions by venipuncture, allowed to clot and centrifuged at 3,000 RPM at 4°C for 10 min and the serum was separated and stored in a frozen state at - 20°C for analysis. Malondialdehyde (MDA) is a marker of lipid peroxidation, Total Anti Oxidant Status (TAOS) and Redox Ratio (RER) [5] markers were assessed by using commercially available kits.

Statistical Analysis: Statistical analyses were performed using Statistical Package for Social Sciences 16. Data expressed as mean ± SD. Independent student's paired 't' test was applied to compare various parameters between groups. The null hypothesis was rejected at p<0.05.

RESULTS

As shown in Table. 1, there were no significant differences in baseline characteristics like age, gender and other anthropometric parameters like height and weight. Table 2, depicts the information about the markers of inflammation like MDA, TAOS and RER. The markers of oxidative stress (MDA, RER) were significantly high (p<0.001) and TAOS was low (p<0.001) in patients suffering from pellagra, when compared to age and gender matched controls.

Table: 1 Physiological characteristics of study participants.

Parameter	Pellagra patients	Controls
Age (Years)	37.34 ± 7.58	38.32 ± 6.4
Men/Women,	42/36	47/31
Height (cm)	163.44 ± 5.24	161.98 ± 6.4
Weight (Kg)	66.23 ± 7.48	67.18 ± 3.48

Table: 2. Difference of Oxidative stress markers.

Parameter	Pellagra patients	Controls
TAOS (mM)	0.40 ± 0.14	0.99 ± 0.33***
MDA (uM)	11.41 ± 9.72	9.08 ± 9.08**
RER	28.52 ± 15.12	9.17 ± 3.9***

*p<0.05, *** p<0.001. TAOS: Total Anti Oxidant Status, MDA: Malondialdehyde, RER: Redox ratio.

DISCUSSION

Oxidative stress occurs if the production of free radicals and active intermediates in a system exceeds the system's capability to neutralize and eliminate them^[6]. The recent concept of "oxidative stress" should also include the pathways related to the "nitrosative stress" and, for their implication in cellular and extracellular metabolic events, to the "metabolic stress". Reactive oxygen intermediate (ROI) and reactive nitrogen intermediate (RNI) are constantly produced under physiological conditions^{[7] [8]}, is the crucial event in living organisms. At the moment, the concept of oxidative stress confined to ROI such as hydroxyl and superoxide radicals, and hydrogen peroxide and singlet oxygen has been extended onto RNI such as nitric oxide (NO), peroxy nitrite and, recently, to S-nitrosothiols^[8]. Thus, ROI and RNI react with proteins, carbohydrates and lipids, with consequent alteration both in the intracellular and intercellular homeostasis, leading to possible cell death and regeneration^[9]. To cope with the oxidative stress elicited by aerobic metabolism, animal and human cells have developed a ubiquitous antioxidant defense system, which consists of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and glutathione reductase together with a number of low molecular-weight antioxidants such as ascorbate, -tocopherol and glutathione, cysteine, thioredoxin, vitamins, etc. However, this antioxidant defense system may be overwhelmed by various pathological or environmental factors so that a fraction of ROS may escape destruction and form the far more reactive hydroxyl radicals (10)(11). An increase in ROS elicited oxidative damage to DNA and other biomolecules may impair normal functions of tissue cells and lead to human aging and disease^{[12][13]}.

In this study, the reduced TAOS, increased MDA and RER indicate that, there was a high level of oxidative stress in pellagra patients.

CONCLUSION

In conclusion, the results of this study showed the increased MDA, RER levels and decreased TAOS levels. Estimation of these markers at early stage will help to take measures to prevent the progression of disease and develop antioxidant strategies.

Limitations: Future studies should include more sample size and more precise oxidative stress markers of pellagra.

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